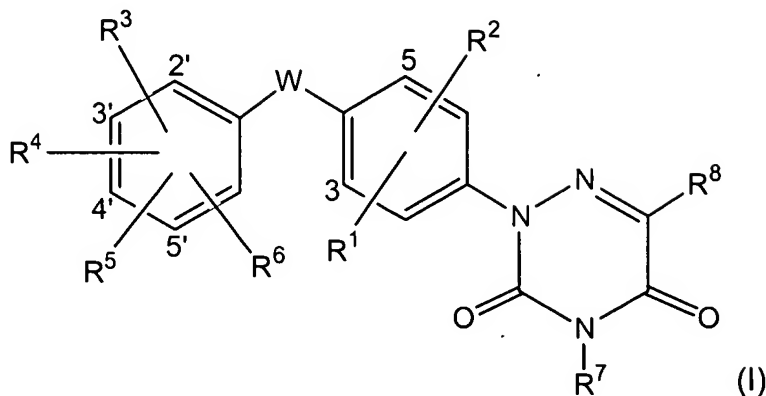


Listing of Claims:

Claim 1 (Original). A compound of Formula I



an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug;
wherein W is (a) -O-, (b) -S(O)_m-, (c) -NR³⁰-, (d) -C(O)-, (e) -HC=CH-, (f) -CH₂-, (g) -CHF-, (h) -CF₂- or (i) -CH(OH)-;

R¹ and R² are independently (a) hydrogen, (b) halogen, (c) -(C₁-C₆)alkyl, (d) -CN, (e) -OR¹² or (f) -trifluoromethyl;

R³ is (a) hydrogen, (b) halogen, (c) -(C₁-C₆)alkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, -OCF₃ and -CF₃, (d) -CN, (e) -OR¹², (f) -trifluoromethyl, (g) -NO₂, (h) -SO₂-R¹³, (i) -C(O)₂R⁹, (j) -C(O)NR¹⁹R²⁰, (k) -C(O)R¹⁶, (l) -NR²¹C(O)-NR²¹R²², (m) -NR¹⁹-C(O)R²⁰ or (n) -NR¹⁷R¹⁸;

R⁴ is (a) -C(R¹⁴)(R¹⁵)(R¹⁶), (b) -(C₀-C₃)alkyl-NR¹⁷R¹⁸, (c) -C(O)NR¹⁹R²⁰, (d) -NR¹⁹-C(O)-R²⁰, (e) -(C₀-C₃)alkyl-NR²¹-C(O)-NR²¹R²², (f) -S(O)_m-R²², (g) -S(O)₂-NR²¹R²², (h) -NR²¹-S(O)₂-R²², (i) -aryl, (j) -het, (k) -OR³³ or (l) halogen; provided that in substituents (f) and (h), R²² is other than -OR³⁴; and provided that when substituent (b) is -(C₀)alkyl-NR¹⁷R¹⁸, R¹⁸ is other than -C(O)-R²⁸ or -S(O)₂-R²⁹;

or R³ and R⁴ may be taken together to form a carbocyclic ring of Formula -(CH₂)_b- or a heterocyclic ring selected from the group consisting of -Q-(CH₂)_c- and -(CH₂)_j-Q-(CH₂)_k- wherein Q is O, S or NR²⁵; wherein said carbocyclic ring is optionally substituted with one or more substituents independently selected from Group V; and wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from Group Z;

R⁵ is -OR²³;

or R⁴ and R⁵ may be taken together to form a heterocyclic ring selected from the group consisting of -CR³¹=CR³²-NH-, -N=CR³¹-NH-, -CR³¹=CR³²-O- and -CR³¹=CR³²-S-;

R⁶ is (a) hydrogen, (b) halogen, (c) -(C₁-C₆)alkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, -OCF₃ and -CF₃, (d) -CN, (e) -OR¹², (f) -trifluoromethyl, (g) -NO₂, (h) -SO₂-R¹³, (i) -C(O)₂R⁹, (j) -C(O)NR¹⁹R²⁰, (k) -C(O)R¹⁶, (l) -NR²¹C(O)NR²¹R²², (m) -NR¹⁹-C(O)R²⁰ or (n) -NR¹⁷R¹⁸;

R⁷ is (a) hydrogen, (b) -(C₁-C₄)alkyl wherein each carbon atom is optionally substituted with 1 to 3 halo atoms or (c) -(CH₂)_nCOOR⁹;

R⁸ is (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -C(O)-OR⁹, (d) -C(O)NR¹⁰R¹¹ or (e) -CN; provided that in substituent (c), R⁹ is other than methyl or ethyl; and provided that in substituent (d), R¹⁰ and R¹¹ are not both hydrogen;

R⁹ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl optionally substituted with phenyl, (c) -(C₂-C₁₂)dialkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R¹⁰ and R¹¹ are independently (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₃-C₁₀)cycloalkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₂-C₁₂)alkenyl or (e) -het;

or R¹⁰ and R¹¹ for any occurrence may be taken together with the nitrogen atom to which are they attached to form het;

R¹² is (a) hydrogen or (b) -(C₁-C₆)alkyl wherein each carbon atom is optionally substituted with 1 to 3 fluoro atoms;

R¹³ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -NR¹⁷R¹⁸, (e) -aryl or (f) -het;

R¹⁴ is (a) hydrogen, (b) -(C₁-C₆)alkyl or (c) -O-R³⁴;

R¹⁵ is (a) hydrogen or (b) -(C₁-C₆)alkyl;

or R¹⁴ and R¹⁵ are taken together with the carbon atom to which they are attached to form a carbonyl group;

R¹⁶ is (a) hydrogen, (b) -(C₁-C₆)alkyl wherein each carbon atom is optionally substituted with 1 to 3 fluoro atoms, (c) -(C₀-C₆)alkyl-(C₃-C₁₀)cycloalkyl, (d) -(C₀-C₆)alkyl-aryl or (e) -(C₀-C₆)alkyl-het;

R¹⁷ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -OR³⁴ or (f) -(C₃-C₁₀)cycloalkyl;

R¹⁸ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -C(O)-R²⁸, (f) -S(O)₂-R²⁹, (g) -OR³⁴ or (h) -(C₃-C₁₀)cycloalkyl;

or R¹⁷ and R¹⁸ for any occurrence are taken together with the nitrogen atom to which they are attached to form het;

R¹⁹ and R²⁰ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₀-C₆)alkyl-aryl, (d) -(C₀-C₆)alkyl-het, (e) -C(O)-NR²⁶R²⁷, (f) -C(O)-R²⁸, (g) -S(O)₂-R²⁹, (h) -OR³⁴ or (i) -(C₃-C₁₀)cycloalkyl;

or R¹⁹ and R²⁰ for any occurrence are taken together with the nitrogen atom to which they are attached to form het;

R²¹ and R²² for each occurrence are independently (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one to three substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -(C₃-C₁₀)cycloalkyl or (f) -OR³⁴;

or R²¹ and R²² are taken together with the nitrogen atom to which they are attached to form het;

R²³ is (a) hydrogen, (b) -(C₁-C₄)alkyl optionally substituted with one or more substituents independently selected from Group V or (c) -C(O)-R²⁴;

R²⁴ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R²⁵ for each occurrence is independently (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -COR²⁹ or (d) -SO₂R²⁹;

R²⁶ and R²⁷ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -(C₀-C₆)alkyl-aryl, or (e) -(C₀-C₆)alkyl-het,

R²⁸ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R²⁹ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -aryl or (e) -het;

R³⁰ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₁-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -C(O)-R³¹ or (f) -S(O)_m-R³²;

R³¹ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl, (f) -het or (g) -OR³⁴;

R³² is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R³³ is (a) -(C₀-C₆)alkyl-aryl, (b) -(C₀-C₆)alkyl-het, (c) -(C₇-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₁-C₆)alkyl wherein at least one carbon atom is substituted with 1 to 3 fluoro atoms, (e) -(C₂-C₁₂)alkenyl or (f) -(C₃-C₁₀)cycloalkyl;

R³⁴ is (a) -aryl, (b) -het, (c) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₂-C₁₂)alkenyl or (e) -(C₃-C₁₀)cycloalkyl;

-(C₃-C₁₀)cycloalkyl for each occurrence is a fully or partially saturated mono-, bi- or tricyclic ring containing three to ten carbon atoms; wherein in the bicyclic ring, a monocyclic cycloalkyl ring is spiro fused to another cycloalkyl ring or is fused via two carbon atoms to a benzene ring or another cycloalkyl ring; and wherein in the tricyclic ring, a bicyclic ring is spiro fused to a cycloalkyl ring or is fused via two atoms to a benzene ring or another cycloalkyl ring;

said -(C₃-C₁₀)cycloalkyl optionally contains one to three bridging atoms independently selected from carbon, oxygen, sulfur and nitrogen; said bridging atoms are attached to two carbon atoms in the ring; and said bridging atoms are optionally substituted with one to three groups independently selected from -(C₁-C₆)alkyl and hydroxy;

said cycloalkyl ring is optionally substituted on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with one or more substituents independently selected from Group V;

Group V is (a) $-(C_1-C_6)alkyl$ optionally substituted with one or two hydroxy, (b) $-(C_2-C_5)alkynyl$, (c) -halogen, (d) $-NR^{35}R^{36}$, (e) $-NO_2$, (f) $-OCF_3$, (g) $-OR^{37}$, (h) $-SR^{37}$, (i) -oxo, (j) -trifluoromethyl, (k) $-CN$, (l) $-C(O)NR^{35}-OH$, (m) $-COOR^{35}$, (n) $-O-C(O)-(C_1-C_6)alkyl$, (o) $-(C_3-C_{10})cycloalkyl$ optionally substituted with CN , (p) $-(C_0-C_6)alkyl-aryl$, (q) $-(C_0-C_6)alkyl-het$, (r) $-C(O)-(C_1-C_6)alkyl$ or (s) $-C(O)-aryl$;

R^{35} and R^{36} for each occurrence are independently (a) hydrogen, (b) $-(C_1-C_6)alkyl$ or (c) $-(C_0-C_6)alkyl-aryl$;

R^{37} is (a) hydrogen, (b) $-(C_1-C_6)alkyl$ optionally substituted with one or more halo, hydroxy or methoxy, (c) $-(C_0-C_6)alkyl-aryl$ or (d) $-(C_0-C_6)alkyl-het$;

aryl is (a) phenyl optionally substituted with one or more substituents independently selected from Group Z; (b) naphthyl optionally substituted with one or more substituents independently selected from Group Z or (c) biphenyl optionally substituted with one or more substituents independently selected from Group Z;

het for each occurrence is a 4-, 5-, 6-, 7- and 8-membered fully saturated, partially saturated or fully unsaturated mono-, bi- or tricyclic heterocyclic ring containing from one to four heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen; wherein in the bicyclic ring, a monocyclic heterocyclic ring is spiro fused to a $-(C_3-C_8)cycloalkyl$ ring or to another heterocyclic ring which is fully or partially saturated; or is fused via two atoms to a benzene ring, a $-(C_3-C_8)cycloalkyl$ ring or another heterocyclic ring; and wherein in the tricyclic ring, a bicyclic ring is spiro fused to a $-(C_3-C_8)cycloalkyl$ ring or to another heterocyclic ring which is fully or partially saturated; or is fused via two atoms to a benzene ring, a $(C_3-C_6)cycloalkyl$ ring, or another heterocyclic ring;

said het optionally contains one to three bridging atoms independently selected from oxygen, sulfur and nitrogen; said bridging atoms are attached to two other atoms in the ring; and said bridging atoms are optionally substituted with one to three groups independently selected from $-(C_1-C_6)alkyl$ and hydroxy;

said het optionally has one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

said het is optionally substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with one or more substituents independently selected from Group Z;

Group Z for each occurrence is independently (a) hydrogen, (b) halogen,

(c) trifluoromethyl, (d) hydroxy, (e) $-\text{OCF}_3$, (f) $-\text{CN}$, (g) $-\text{NO}_2$, (h) $-(\text{C}_1-\text{C}_6)\text{alkyl}$ optionally substituted with one or more substituents independently selected from the group consisting of hydroxy, halogen, $-\text{OCF}_3$ and $-\text{CF}_3$, (i) $-(\text{C}_2-\text{C}_6)\text{alkenyl}$ optionally substituted with phenyl, (j) $-(\text{C}_2-\text{C}_5)\text{alkynyl}$, (k) $-(\text{C}_1-\text{C}_6)\text{alkoxy}$, (l) $-(\text{C}_0-\text{C}_6)\text{alkyl-phenyl}$ optionally substituted with one or more substituents independently selected from the group consisting of halogen, $-\text{OCF}_3$, $-\text{CF}_3$, $-(\text{C}_1-\text{C}_4)\text{alkyl}$, $-(\text{C}_1-\text{C}_4)\text{alkoxy}$ and $-\text{C}(\text{O})\text{CH}_3$, (m) $-(\text{C}_0-\text{C}_6)\text{alkyl-naphthyl}$ optionally substituted with one or more substituents independently selected from the group consisting of halogen, $-\text{OCF}_3$, $-\text{CF}_3$, $-(\text{C}_1-\text{C}_4)\text{alkyl}$, $-(\text{C}_1-\text{C}_4)\text{alkoxy}$ and $-\text{C}(\text{O})\text{CH}_3$, (n) $-\text{C}(\text{O})_2\text{R}^{35}$, (o) $-(\text{C}_0-\text{C}_6)\text{alkyl-C}(\text{O})\text{NR}^{35}\text{R}^{36}$, (p) $-(\text{C}_0-\text{C}_6)\text{alkyl-C}(\text{O})\text{R}^{38}$, (q) $-\text{NR}^{35}\text{R}^{36}$, (r) $-\text{NR}^{35}-\text{C}(\text{O})\text{NR}^{35}\text{R}^{36}$, (s) $-\text{NR}^{35}-\text{C}(\text{O})\text{R}^{36}$, (t) $-\text{OR}^{37}$, (u) $-\text{SR}^{37}$, (v) $-(\text{C}_3-\text{C}_{10})\text{cycloalkyl}$, (w) $-(\text{C}_0-\text{C}_6)\text{alkyl-pyridinyl}$ optionally substituted with one or more $-(\text{C}_1-\text{C}_6)\text{alkyl}$ which is optionally substituted with one or more substituents independently selected from the group consisting of hydroxy and halo, (x) $-(\text{C}_0-\text{C}_6)\text{alkyl-piperidinyl}$ optionally substituted with one or more $-(\text{C}_1-\text{C}_6)\text{alkyl}$ which is optionally substituted with one or more substituents independently selected from hydroxy and halo, (y) $-\text{SO}_2-\text{R}^{37}$, (z) $-\text{SO}_2-\text{NR}^{35}\text{R}^{36}$ or

(a1) $-\text{S-phenyl-CH}_2\text{OH}$;

R^{38} is (a) $-(\text{C}_1-\text{C}_6)\text{alkyl}$, (b) $-(\text{C}_0-\text{C}_6)\text{alkyl-phenyl}$, (c) $-(\text{C}_0-\text{C}_6)\text{alkyl-phenanthrenyl}$ optionally substituted with one to three CF_3 , (d) $-(\text{C}_0-\text{C}_6)\text{alkyl-pyrrolidinyl}$ or (e) $-(\text{C}_0-\text{C}_6)\text{alkyl-morpholinyl}$;

or any two Z Groups for any occurrence in the same variable may be taken together to form (a) a carbocyclic ring of the formula $-(\text{CH}_2)_e-$ or (b) a heterocyclic ring selected from the group consisting of $-\text{O}(\text{CH}_2)_f\text{O}-$, $-(\text{CH}_2)_g\text{NH}-$ and $-\text{CH}=\text{CHNH}-$;

m is 0, 1 or 2;

n is 0, 1, 2 or 3;

b is 3, 4, 5, 6 or 7;

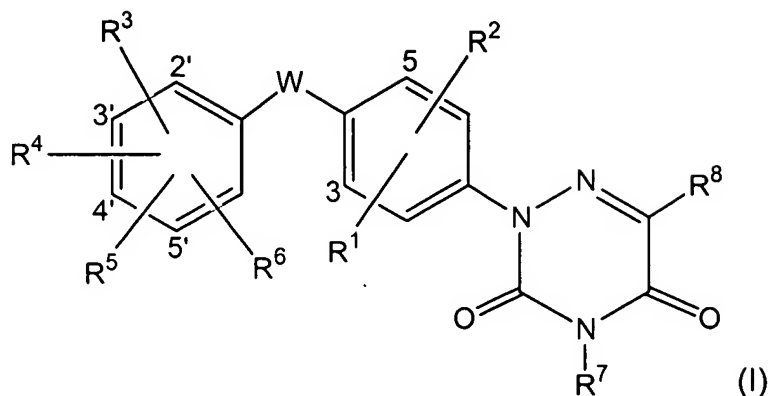
c, f, g, j and k are each independently 2, 3, 4, 5 or 6; and

e is 3, 4, 5, 6 or 7;

provided that in a compound of Formula I: 1) the substituent $-\text{C}(\text{R}^{14})(\text{R}^{15})(\text{R}^{16})$ in R^4 is other than $(\text{C}_1-\text{C}_4)\text{alkyl}$; and 2) R^4 is halo only when R^8 is $-\text{C}(\text{O})-\text{OR}^9$ or $-\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$.

Claims 2-54 (Cancelled).

Claim 55 (New). A compound of the formula:



or a pharmaceutically acceptable salt of said compound, in which:

W is -O-,

R¹ is located at the 3-position and is selected from methyl, bromo, or chloro,

R² is located at the 5-position and is selected from methyl, bromo, or chloro,

R³ is located at the 2' position and is represented by hydrogen,

R⁴ is located at the 3' position and is represented by -C(R¹⁴)(R¹⁵)(R¹⁶),

R⁵ is located at the 4' position and is represented by hydroxy or methoxy,

R⁶ is located at the 5' position and is represented by hydrogen,

R⁷ is hydrogen,

R⁸ is hydrogen,

R¹⁴ is hydrogen, or -(C₁-C₆) alkyl,

R¹⁵ is hydrogen or -(C₁-C₆) alkyl,

R¹⁶ is -(C₀-C₆)alkyl-aryl,

aryl is (a) phenyl optionally substituted with one or more substituents independently selected from Group Z; (b) naphthyl optionally substituted with one, or more substituents independently selected from Group Z or (c) biphenyl optionally substituted with one or more substituents independently selected from Group Z, and;

Group Z, for each occurrence, is independently selected from the group consisting of (a) hydrogen, (b) halogen, (c) trifluoromethyl, (d) hydroxy, (e) -OCF₃, (f) -CN, (g) -NO₂, and (h) -(C₁-C₆)alkyl.

Claim 56 (New). A compound according to claim 55 in which R¹ and R² are each methyl.

Claim 57 (New) A compound according to claim 55 in which R⁵ is hydroxy.

Claim 58 (New). A compound according to claim 55 in which R¹⁶ is (C₀)alkyl-aryl.

Claim 58 (New) A compound according to claim 58 in which aryl is phenyl, optionally substituted with one or more substituents independently selected from Group Z.

Claim 59 (New) A compound according to claim 55 selected from the group consisting of:

- i) 2-{3-chloro-4-[3-(4-fluoro-benzyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-2H [1,2,4]triazine-3,5-dione;
- ii) 2-{4-[3-(4-fluoro-benzyl)-4-methoxy-phenoxy]-3,5-dimethyl-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- iii) 2-(4-{3-[(4-fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-3,5-dimethyl-phenyl)-2H-[1,2,4]triazine-3,5-dione;
- iv) 2-{4-[3-(4-fluoro-benzyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2H-[1,2,4]triazine-3,5-dione
- v) 2-{3,5-dichloro-4-[3-(4-fluoro-benzyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione, and;
- vi) 2-{3,5-dibromo-4-[3-(4-fluoro-benzyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione

Claim 60 (New). A pharmaceutical composition comprising an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt of said compound, in admixture with a pharmaceutically acceptable carrier.

Claim 61 (New). 2-{4-[3-(4-Fluoro-benzyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2H-[1,2,4]triazine-3,5-dione, or a pharmaceutically acceptable salt of said compound.

Claim 62 (New). A topical pharmaceutical composition comprising an effective amount of a compound of claim 61, in admixture with a pharmaceutically acceptable topical carrier.